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Prognostic value of troponin T in hemodialysis patients is independent of comorbidity

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Prognostic value of troponin T in hemodialysis patients is independent of comorbidity.

Background. Patients on long-term hemodialysis have a high mortality. Various clinical and biochemical markers are of prognostic value. Cardiac troponin T (cTnT) is a sensitive and specific marker for myocardial damage. Asymptomatic dialysis patients have a high prevalence of cTnT concentrations above the diagnostic threshold for myocardial damage. There is controversy over whether this represents a false positive cTnT or an underlying pathology with a poor outcome. It is not known whether cTnT reflects comorbidity in these patients.

Methods. A cohort of 73 long-term hospital hemodialysis patients had cTnT estimated once prior to a mid-week dialysis. Samples were analyzed using the second-generation cTnT assay from Boehringer Mannheim on an Elecsys 1010 analyzer. The standard diagnostic threshold for myocardial damage of 0.1 ng/mL was used. A commonly employed measure of comorbidity (Khan) was applied at the time cTnT was measured. Patients were followed for 15 months. Mortality was used as the clinical end point. Kaplan-Meier survival analysis was employed and differences between groups were assessed using the Cox-Mantel log-rank test.

Results. Of the 73 patients, 20 were positive for cTnT and 53 were negative, at the cut-off of 0.1 ng/mL. At fifteen months, 65% of the positive patients were dead, whereas only 15% of the negative patients were dead. Survival analysis confirmed that this difference was statistically significant ($P < 0.00001$), and that the effect of cTnT on survival was independent of comorbidity.

Conclusions. There is a high prevalence of positive cTnT in stable hemodialysis patients. A single estimation of cTnT in this group has significant prognostic value, independent of comorbidity.

Key words: survival analysis, end-stage renal failure, cardiovascular disease, ischemic heart disease, peripheral vascular disease, acute myocardial infarction.

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Cardiac troponin T (cTnT) is a sensitive and specific marker of myocardial damage [1]. It is used in the diagnosis of acute myocardial infarction (AMI) and in the risk-stratification of patients with unstable angina pectoris [2].

Patients on hemodialysis for end-stage chronic renal failure have a high mortality, much of it related to cardiovascular disease, including AMI. The specificity of cTnT in the diagnosis of AMI in hemodialysis patients and in diabetes has been questioned. The first generation assay for cTnT demonstrated a very high prevalence of positive cTnT values in these patients, in the order of 80% [3]. Despite the lack of specificity, a positive first generation cTnT has been associated with a poor prognosis in hemodialysis patients [3]. The second generation assay, utilizing two monoclonal antibodies, is more specific for myocardial damage. Nevertheless, a proportion of hemodialysis patients (20 to 50%) remains, with serum cTnT concentration above the diagnostic cut-off point for myocardial damage (0.1 ng/mL) [4–7]. Several reports have suggested that elevated second generation cTnT is associated with a poor prognosis [5, 8–12]. Other studies have failed to detect such an effect [13, 14]. If there is an association between cTnT and prognosis in hemodialysis patients, it remains to be demonstrated that this is independent of the clinical factors that are already known to influence survival. These include age, length of time on dialysis, the presence of diabetes, ischemic heart disease, left ventricular hypertrophy, and other comorbid conditions. Various clinical scores are used to stratify hemodialysis patients according to comorbidity [15]. These are used to compare outcomes in dialysis populations. One such scoring system is that of Khan and co-workers, which has been shown to correlate with outcome (Table 1) [16]. If cTnT is of prognostic value in hemodialysis patients, the optimal cut-off point (diagnostic threshold) of serum cTnT concentration remains to be established.

This study aimed to establish whether cTnT is a prognostic marker in hemodialysis patients, and whether any prognostic information is independent of an established

Table 1. Comorbidity scoring system[a]

Risk group	Inclusion criteria
Low	Age <70 years and no comorbid illness
Medium	Age 70–80 years or Age <80 years with any one of the following: angina, previous myocardial infarction, cardiac failure, chronic obstructive airways disease, pulmonary fibrosis, liver disease (cirrhosis, chronic hepatitis)
High	Age >80 years or Any age with two or more organ dysfunctions in addition to end-stage renal disease or Any age with diabetes or cardiopulmonary disease or Any age with visceral malignancy

[a]This clinical prognostic scoring system was developed by Khan et al [16]

prognostic index. A further aim of the study was to determine the optimal prognostic cut-off concentration of cTnT.

METHODS

Study design

Survival of a group of 73 patients on long-term hospital hemodialysis was examined. The total hospital population of chronic hospital hemodialysis patients was 81. Blood samples suitable for the analysis of cTnT were available for 73 patients. Each patient had cTnT estimated once. cTnT estimation was completed for all patients within a three-day period. This study used the standard laboratory cut-off point for the diagnosis of myocardial damage of 0.1 ng/mL. Patients were followed up for 15 months. Clinical details were obtained at the end of the period by review of clinical notes by a nephrologist familiar with the patients, but unaware of the cTnT results. The patients were categorized according to the clinical prognostic scoring system of Khan and co-workers [16], applied at the time at which the sample was taken for cTnT (Table 1). A subgroup analysis was performed of patients who were expected to have a higher prevalence of cTnT. These included 12 patients with diabetes, 18 patients with symptomatic ischemic heart disease (IHD) and 23 patients with known peripheral vascular disease (PVD).

Echocardiograms were performed as part of routine clinical care in 57 of the patients and were performed by a number of different technicians. Data was extracted from the clinical notes and by searching the echocardiography database. Assessment of left ventricular hypertrophy (LVH) and of left ventricular systolic function (LVSF) was based on the interpretation of the cardiologist reporting the echocardiogram.

Table 2. Patient demographics

Characteristic	
Sex ratio *male:female*	42:31
Diabetes	$N = 12$
Peripheral vascular disease	$N = 23$
Ischemic heart disease	$N = 18$
Age *years, range; median (SD)*	23–91, 64 (18)
Length of time on RRT *months, range*	1–120

Analytical methods

Cardiac troponin T was estimated using the second-generation Elecsys Troponin T STAT immunoassay from Boehringer Mannheim, on the Elecsys 1010 immunoassay analyzer. The detection limit of the assay is 0.01 ng/mL. The coefficient of inter-assay analytical variation in our hands, at the cut-off point of 0.1 ng/mL, was <6%. Urea reduction ratio (URR) was calculated as the difference between the serum urea concentration pre- and post-dialysis, divided by the serum urea pre-dialysis.

Statistical methods

Kaplan-Meier survival analysis was performed. Differences in survival between groups were analyzed using the Cox-Mantel log rank test. The Cox regression model was used to compare the predictive value of cTnT and the clinical scoring system. Receiver operating characteristic (ROC) curve analysis was used to determine the cut-off point that maximized both sensitivity and specificity. The diagnostic efficiency (true positives plus true negatives, divided by total number of tests) of the test at different cut-off points was plotted to determine the cut-off point that correctly assigned the greatest number of patients.

Patients

Patient characteristics are shown in Table 2.

There was a broad range of ages and lengths of time on renal replacement therapy (RRT). There was a male predominance.

RESULTS

Distribution of cTnT

Twenty patients out of seventy-three had serum cTnT greater than 0.1 ng/mL. The distribution of cTnT results is shown in Figure 1. There was no significant correlation between cTnT and urea reduction ratio ($r = -0.1033$, $P = 0.4$).

Outcome

After 15 months of follow-up, 21 patients had died, leaving 52 survivors. The prevalence of cTnT greater than, and less than, the cut-off point of 0.1 ng/mL and their respective survival to 15 months is shown in Table 3. Prevalence of positive cTnT and survival in the following

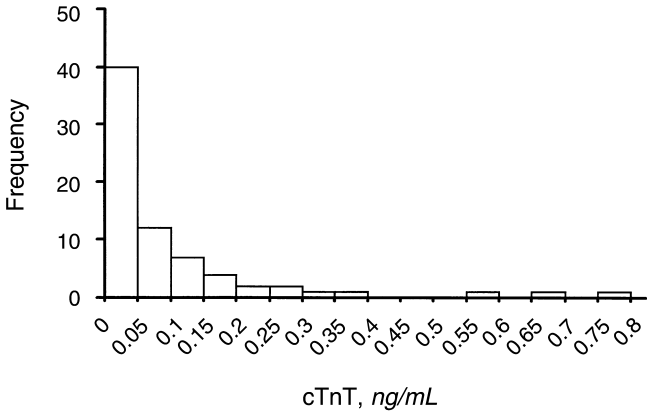

Fig. 1. Frequency histogram of cardiac troponin T (cTnT) concentration in 73 hemodialysis patients.

patient groups is also shown in the Table 3: patients in the low-, medium- and high-risk groups, diabetic patients, patients with symptomatic ischemic heart disease and patients with known peripheral vascular disease. In each subgroup those with a negative cTnT had a better outcome. The distribution of cTnT and of survival within groups, divided according to echocardiographic findings, is shown in Table 4. Within the group with left ventricular hypertrophy (LVH) and within the group of patients with good left ventricular systolic function (LVSF), a positive cTnT was a marker of poor outcome. Patients with impaired left ventricular systolic function had a very poor prognosis irrespective of cTnT.

Survival analysis

The Kaplan-Meier survival curve of the 73 patients, divided into those who were cTnT positive and negative is shown in Figure 2. The difference in survival was statistically significant ($P < 0.00001$, Cox-Mantel log-rank test). The survival curve of the 73 patients divided according to the comorbidity score into three groups (low, medium and high risk) is shown in Figure 3. The difference in survival between the groups was statistically significant ($P < 0.0001$, Cox-Mantel log-rank test).

To make a valid comparison between cTnT and co-morbidity as predictors of mortality, we expressed both indices as binary variables (cTnT positive versus cTnT negative: High-risk versus medium- and low-risk groups combined). Kaplan-Meier survival analysis was performed for the 43 patients in the combined low and medium risk groups, and is shown in Figure 4. The number of events in the low risk group was too low to allow survival analysis according to cTnT status. The survival analysis for the 30 high risk patients is shown in Figure 5. In both subgroups cTnT was a significant predictor of mortality ($P < 0.001$ and $P < 0.05$, respectively).

Cox regression model

The Cox regression model was used to compare the predictive value of the comorbidity score and cTnT as binary variables, described above. It demonstrated that both variables were significant independent predictors of mortality and that the hazard ratio associated with a high risk comorbidity score was 6.7 (compared with medium and low risk combined), and the hazard ratio associated with a positive cTnT (compared with a negative cTnT) was 4.1.

Cause of death

Cause of death was established in the twenty-one who died, by review of clinical notes. There was no evidence of any tendency for cTnT positive patients to have a cardiac, as opposed to a non-cardiac death. Classified as cardiac were the following deaths: two myocardial infarctions, six cardiac arrests and four cases of cardiac failure. Classified as non-cardiac were the following deaths: four withdrawals from dialysis treatment as a result of severe intractable comorbidity, four cases of sepsis and one malignancy. The distribution of cTnT among the cardiac and non-cardiac causes of death is shown in Table 5.

Determination of cut-off points

The receiver operating characteristic (ROC) curve for cTnT as a predictor of death at 15 months is shown in Figure 6. The area under the ROC curve was 0.857, standard error 0.055, 95% confidence interval 0.755 to 0.928. The point at which sensitivity and specificity were equal (at 76%) was at cTnT concentration of 0.063 ng/mL.

In terms of diagnostic efficiency, the proportion of patients correctly assigned (true positives plus true negatives divided by total), there was essentially no difference between cut-off points between 0.06 and 0.2 ng/mL (Fig. 7). The Cox regression model was repeated to assess whether the 0.06 ng/mL cut-off point performed better than the 0.1 ng/mL cut-off point. This demonstrated that when using the 0.06 ng/mL cut-off point, the hazard ratio associated with a positive cTnT was 4.8, while the hazard ratio associated with a high risk score was reduced to 4.3.

DISCUSSION

The high prevalence of raised cTnT in asymptomatic dialysis patients undermines the role of this marker in the diagnosis of acute coronary syndromes in this group of patients. Cardiac troponin I has been shown to be a better predictor of acute myocardial damage than troponin T, in dialysis patients who present with chest pain [17]. Van Lente and co-workers found that in a group of renal patients (only 9% of whom were dialysis-dependent) who presented with chest pain, both cTnT and TnI

Table 3. Prevalence of cTnT above and below the cut-off point in 73 hemodialysis patients and in sub-groups of those patients, and their respective survival to 15 months

	Number			Survival %		
Group	Total	cTnT >0.1 ng/mL	cTnT <0.1 ng/mL	Total	cTnT >0.1 ng/mL	cTnT <0.1 ng/mL
All	73	20	53	71	35	85
Low risk	21	1	20	100	100	100
Medium risk	22	6	16	82	50	94
High risk	30	13	17	43	23	59
Diabetes	12	7	5	50	29	80
IHD	18	8	10	61	25	90
PVD	23	13	10	48	31	70

Abbreviations are: cTnT, cardiac troponin T; IHD, ischemic heart disease; PVD, peripheral vascular disease.

Table 4. Prevalence of left ventricular hypertrophy (LVH) and left ventricular systolic function (LVSF) in 73 hemodialysis patients, cTnT above and below the cut-off point in these groups, and their respective survival to 15 months

	Number			Survival %		
Group	Total	cTnT >0.1 ng/mL	cTnT <0.1 ng/mL	Total	cTnT >0.1 ng/mL	cTnT <0.1 ng/mL
LVH	31	11	20	52	9	75
No LVH	11	2	9	91	50	100
No LVH data	31	7	24	84	71	88
Poor LVSF	11	7	4	45	43	50
Good LVSF	44	11	33	70	18	88
No LVSF data	18	2	16	89	100	88

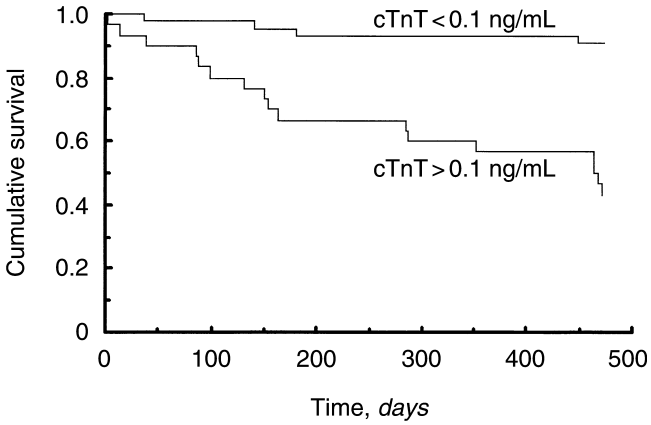

Fig. 2. Kaplan-Meier survival curve of 73 hemodialysis patients according to cardiac troponin T concentration.

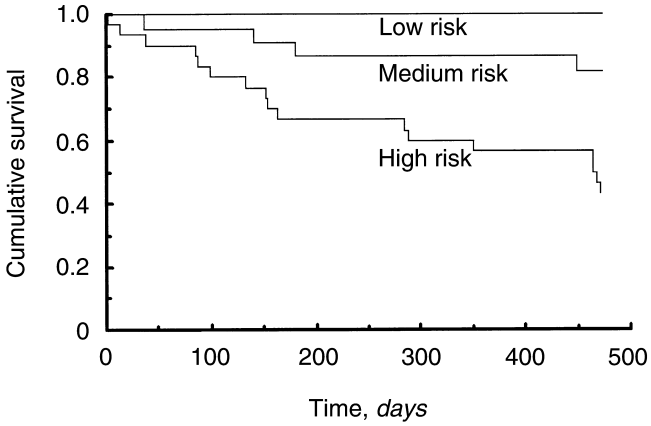

Fig. 3. Kaplan-Meier survival curve of 73 hemodialysis patients according to Khan comorbidity score.

predicted adverse outcomes less well than in non-renal patients [18].

We have demonstrated that a single estimation of cTnT is a predictor of mortality in chronic hemodialysis patients, independent of a commonly used clinical prognostic index. Khan and co-workers used their clinical score at the start of dialysis. We modified the use of the comorbidity score by applying it at the time of the estimation of cTnT. Since cTnT was measured at a single time point, which for these patients was at varying stages in the natural history of their disease, we believed it was appropriate to compare the prognostic value of cTnT with comorbidity at the same time.

Use of the Cox regression model in our study was limited to estimating the relative strength of cTnT and the clinical comorbidity score in predicting death in dialysis patients. We did not seek to determine the best model to predict death in these patients, and thus no other biochemical and clinical factors were included in the model. Patients were grouped so that both the clinical score and cTnT status would be in a binary format, so that like

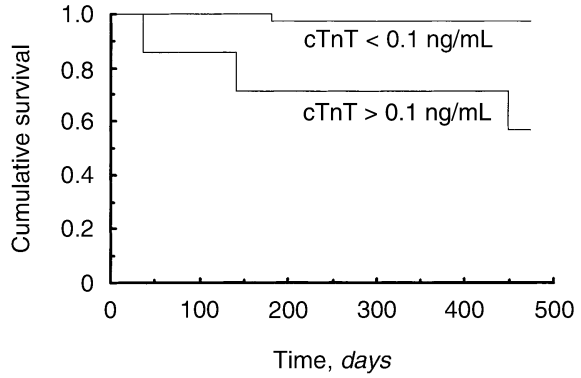

Fig. 4. Kaplan-Meier survival curve of 43 low- and medium-risk hemodialysis patients according to cardiac troponin T concentration.

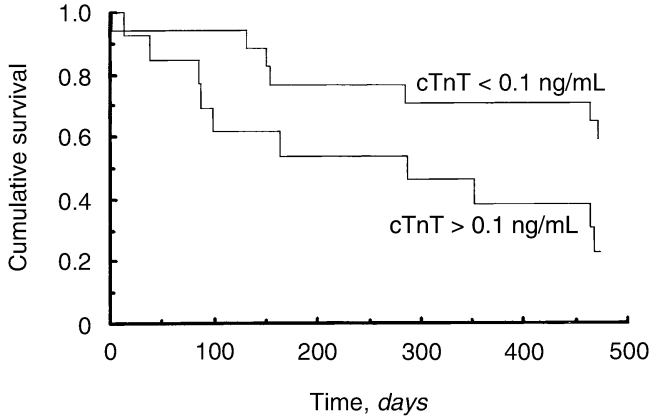

Fig. 5. Kaplan-Meier survival curve of 30 high-risk hemodialysis patients according to cardiac troponin T concentration.

Table 5. Cause of death and cardiac troponin T status among the 21 patients who died

Cause	cTnT >0.1 ng/mL	cTnT <0.1 ng/mL	Total
Cardiac	7	5	12
Non-cardiac	6	3	9
Total	13	7	21

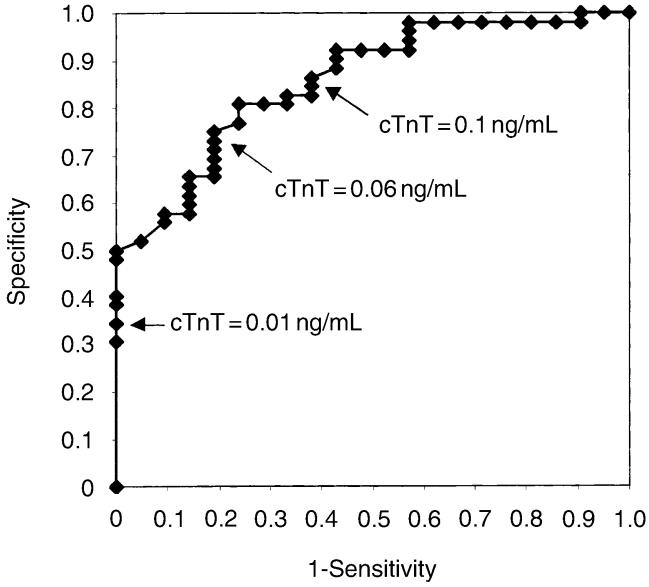

Fig. 6. Receiver operating characteristic (ROC) curve for cardiac troponin T concentration as a predictor of death at 15 months in 73 hemodialysis patients.

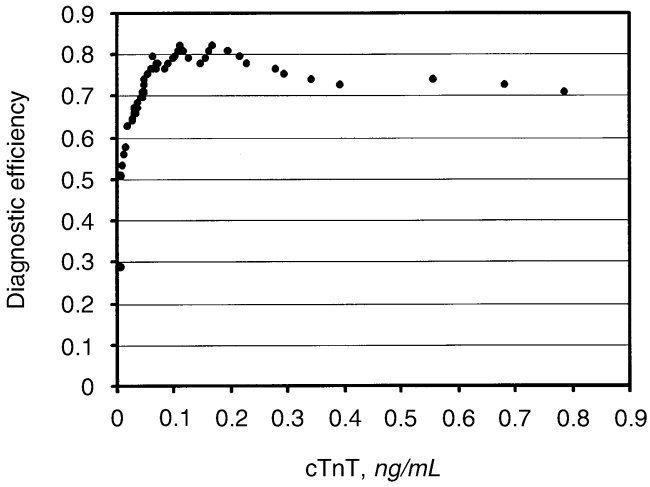

Fig. 7. Diagnostic efficiency of cardiac troponin T as a predictor of death at 15 months, as a function of cardiac troponin T concentration.

could be compared with like, as well as to express the outcome of the analysis in the form of hazard ratios.

Previous studies have shown that cTnT is a predictor of mortality in dialysis patients, independent of certain selected single diagnoses, such as diabetes or vascular disease [8, 11, 19]. Those authors did not evaluate whether cTnT contributed prognostic information in addition to what was obtained from recognized clinical prognostic indices. The cTnT testing protocol in the first of these studies was different to ours. Those authors measured cTnT on three occasions and used the highest concentration, and thus had a higher prevalence of positive patients.

A further study, which demonstrated that cTnT had no effect on prognosis in chronic renal failure, examined a diverse group of patients and included only 20 hemodialysis patients [13]. Mockel et al excluded patients with symptoms of ischemic heart disease, thus selecting a low-risk population. In our study, the patients in the lowest risk group had a very favorable prognosis and a low prevalence of positive cTnT concentration, making it difficult to assess whether a negative cTnT confers a survival advantage in this group with the lowest risk score. We noted that patients with a history of ischemic heart disease, but without recent symptoms suggestive

of an acute coronary syndrome, who were negative for cTnT, had a good prognosis. We believe that these patients should be included in studies into the prognostic value of cTnT in dialysis patients.

This study demonstrated that the cut-off point of 0.1 ng/mL, as is used in the risk stratification of unstable angina, is a reasonable cut-off point for predicting outcome in hemodialysis patients. This cut-off point is close to the point on the ROC curve where sensitivity and specificity are maximal. It also falls within the range in which good diagnostic efficiency is obtained. Larger studies may be required to define the cut-off point with the greatest diagnostic efficiency more precisely. The finding that diagnostic efficiency is maximal at a higher cut-off point than that determined by ROC curve analysis is a reflection of the fact that survival was, overall, a more likely outcome than death in this group. Thus, one was more likely to be correct if one predicted survival rather than death. Choosing a higher cut-off point is the equivalent of predicting more survivors. Unlike analysis of diagnostic efficiency, ROC curve analysis, by emphasizing sensitivity and specificity, does not take into account the prevalence of the outcome in question.

The fact that the 0.06 ng/mL cut-off point emerged as a better predictor using the Cox model suggests that the prognostic information provided by cTnT at lower concentrations is more independent of clinical markers of comorbidity than at higher cTnT concentrations. If one is interested in using cTnT as an additional factor in a panel of clinical and biochemical markers of prognosis (and if one chooses to express cTnT as a binary variable), then the 0.06 ng/mL cut-off point would be preferable to the 0.1 ng/mL cut-off point as it contributes more independent information.

The biological process underlying the increased cTnT in hemodialysis patients is unclear. Several hypotheses have been proposed. It has been suggested that the skeletal myopathy associated with end-stage renal failure induces expression of the fetal isoform, which happens to be cTnT, in replicating skeletal muscle, and that this gives rise to the false-positive cTnT result. This hypothesis has been disputed [20, 21]. It also has been suggested that the presence of left ventricular hypertrophy, silent ischemia, and metabolic cardiomyopathy may cause this elevation of cTnT in dialysis patients. In a diverse group of patients who underwent post-mortem examination and who included a small number of dialysis patients, antemortem cTnT was associated with a range of abnormal myocardial histologic findings [22]. The independent association between cTnT and death in hemodialysis patients would seem to favor a cardiac pathology. Ooi et al [11], in contrast with their findings at twelve months of follow-up, found that follow-up at thirty-six months demonstrated that a positive cardiac Troponin T was associated with cardiac—as opposed to non-cardiac—death. A similar association between cardiac Troponin T and fatal cardiovascular events was found by Dierkes and co-workers [19].

In our study, however, there did not appear to be a relative excess of cardiac, as opposed to non-cardiac, death among the cTnT positive patients. The cause of death was determined by review of case notes and no post-mortem examinations were performed. Sudden, unexpected death at home, one of the principal modes of death in these patients, was classified as cardiac arrest. This relatively crude and limited analysis should not be expected to correlate closely with detailed post-mortem examinations.

The discrepancy between the prevalence of positive cTnT and cTnI in dialysis patients has been debated [21]. It is known that cTnI has a shorter serum half-life. It also is known that the two epitopes on the cTnT molecule that are recognized by the current cTnT assay are very close together and thus make the assay quite resistant to instability on storage. Cleavage of the molecule must occur between the two epitopes for the molecule to fail to react in the assay system. The epitopes recognized by most of the various cTnI assay systems are situated further apart on the molecule. Thus, proteolytic degradation products of cTnT are much more likely to be detected by the cTnT assay than are cTnI degradation products in the cTnI assay systems. Wu and co-workers speculate that retention of proteolytic degradation products of cTnT in dialysis patients, which are detected by the cTnT assay, may make the cTnT assay more sensitive to minor degrees of myocardial damage [23]. Thus, they suggest that the signal caused by minor ongoing myocardial damage is amplified in the case of cTnT in dialysis patients, but not in the case of cTnI.

Predicting survival in renal dialysis patients is important. When comparing clinical outcomes between different renal units, as part of benchmarking exercises, it is essential to correct for the underlying comorbidity and for the prognosis of the patients [16]. Clinical prognostic factors have been thoroughly explored. Biochemical prognostic factors such as C-reactive protein may add to the ability to predict outcome [24]. cTnT may, in the future, be included in a panel of biochemical markers used to assist in this process. The concept of rationing dialysis on the basis of prognosis has been opened for debate [15]. Other treatment options may also be considered in the light of a patient's prognosis, such as referral for revascularization procedures or renal transplantation. In our study, dialysis patients with left ventricular hypertrophy (LVH) who had a positive cardiac Troponin T had a much worse prognosis than similar patients with negative cTnT. This difference suggests that it might be possible target therapy aimed at inducing regression of LVH at those patients with the poorest prognosis, that is, those with a positive cTnT.

Issues deserving further study include the pathophysiological basis, the biological variation, and kinetic behavior of cTnT in end-stage renal disease. Ultimately, cTnT may help identify those patients who would benefit from intervention.

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REFERENCES

1. Collinson P: Troponin T or Troponin I, or CK-MB (or none?). *Eur Heart J* 19:N16–N24, 1998
2. Stubbs P: The cardiac troponins: Uses in routine clinical practice. *Eur Heart J* 19:N59–N63, 1998
3. Apple F, Sharkey S, Hoeft P, *et al*: Prognostic value of serum cardiac troponin I and T in chronic dialysis patients: A 1-year outcomes analysis. *Am J Kidney Dis* 29:399–403, 1997
4. Lowbeer C, Ottosson-Seeberger A, Gustafsson S, *et al*: Increased cardiac troponin T and endothelin-1 concentrations in dialysis patients may indicate heart disease. *Nephrol Dial Transplant* 14:1948–1955, 1999
5. McNeil A, Marshall M, Ellis C, Hawkins R: Why is Troponin T increased in the serum of patients with end-stage renal disease. (letter) *Clin Chem* 44:2377–2378, 1998
6. Ooi D, House A: Cardiac troponin T in haemodialysed patients. *Clin Chem* 44:1410–1416, 1998
7. Willning S, Keller F, Steinbach G: Specificity of cardiac Troponins I and T in renal disease. *Clin Chem Lab Med* 36:87–92, 1998
8. Stolear J, Georges B, Shita A, Verbeelen D: The predictive value of cardiac troponin T measurements in subjects on regular dialysis. *Nephrol Dial Transplant* 14:1961–1967, 1999
9. Roppolo L, Fitzgerald R, Dillow J, *et al*: A comparison of troponin T and troponin I as predictors of cardiac events in patients undergoing chronic dialysis at a Veteran's Hospital: A pilot study. *J Am Coll Cardiol* 34:448–454, 1999
10. Porter G, Norton T, Bennett W: Troponin T: A predictor of death in chronic haemodialysis patients. *Eur Heart J* 19:N34–N37, 1998
11. Ooi D, Zimmerman D, Graham J, Wells G: Cardiac troponin T predicts long-term outcomes in haemodialysis patients. *Clin Chem* 47:412–422, 2001
12. Wayand D, Baum H, Schatzle G, *et al*: Cardiac troponin T and I in end-stage renal failure. *Clin Chem* 46:1345–1356, 2000
13. Mockel M, Schindler R, Knorr L, *et al*: Prognostic value of cardiac troponin T and I elevations in renal disease patients without acute coronary syndromes: A 9-month outcome analysis. *Nephrol Dial Transplant* 14:1489–1495, 1999
14. Musso P, Cox I, Vidano E, *et al*: Cardiac troponin elevations in chronic renal failure: Prevalence and clinical significance. *Clin Biochem* 32:125–130, 1999
15. Chandna S, Schulz J, Lawrence C, *et al*: Is there a rationale for rationing chronic dialysis? A hospital based cohort study of factors affecting survival and morbidity. *BMJ* 318:217–223, 1999
16. Khan I, Catto G, Edward N, *et al*: Influence of coexisting disease on survival on renal-replacement therapy. *Lancet* 341:415–418, 1993
17. Martin G, Becker B, Schulman G: Cardiac troponin-I accurately predicts myocardial injury in renal failure. *Nephrol Dial Transplant* 13:1709–1712, 1998
18. Van Lente F, McErlean ES, DeLuca S, *et al*: Ability of troponins to predict adverse outcomes in patients with renal insufficiency and suspected acute coronary syndromes: A case-matched study. *J Am Coll Cardiol* 33:471–478, 1999
19. Dierkes J, Domrose U, Westphal S, *et al*: Cardiac troponin T predicts mortality in patients with end-stage renal disease. *Circulation* 102:1964–1969, 2000
20. Apple F, Ricchiuti V, Voss E, *et al*: Expression of cardiac troponin T isoforms in skeletal muscle of renal disease patients will not cause false-positive serum results by the second generation cardiac troponin T assay. *Eur Heart J* 19:N30–N33, 1998
21. Haller C, Zehelein J, Remppis A, *et al*: Cardiac troponin T in patients with end-stage renal disease: Absence of expression in truncal skeletal muscle. *Clin Chem* 44:930–938, 1998
22. Ooi D, Isotal P, Veinot J: Correlation of antemortem serum creatine kinase, creastine kinase-MB, troponin I and troponin T with cardiac pathology. *Clin Chem* 46:338–344, 2000
23. Wu A, Feng Y: Biochemical differences between cTnT and cTnI and their significance for diagnosis of acute coronary syndromes. *Eur Heart J* 19:N25–N29, 1998
24. Iseki K, Tozawa M, Yoshi S, Fukiyama K: Serum C-reactive protein (CRP) and risk of death in chronic haemodialysis patients. *Nephrol Dial Transplant* 14:1956–1960, 1999